

STUDIES IN HUMAN INHERITANCE XX. FOUR SETS OF ALLELES TESTED FOR INCOMPLETE SEX LINKAGE

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It has long been known that in certain organisms some sex-linked genes are restricted to the X chromosome, others to the Y chromosome, while still others are found both in X and Y chromosomes, with consequent crossing over. In these organisms (e. g., certain fishes) there are thus three kinds of sex linkage: ordinary sex linkage (X chromosome factors), Y chromosome inheritance, and incomplete or partial sex linkage (factors on both X and Y).

Ordinary sex linkage and Y chromosome inheritance have long been known in man. Some thirty genes are known to be sex linked in the ordinary way, and four or five genes are known to be restricted to the Y chromosome. The latter include the genes for one type of webbed toes, ichthyosis hystrix gravior, dense black hair on the entire ear, and hard round projecting skin lesions.

Koller and Darlington (1934) demonstrated that the sex chromosomes of mammals might also be expected to carry genes which occur on both X and Y with crossing over, since chiasmata occur between homologous portions of these chromosomes. The sex chromosomes therefore are constituted as follows: one portion of the X is non-homologous, carrying ordinary sex linked genes; the rest is homologous with a corresponding portion of the Y, and these homologous portions may carry genes which would be incompletely sex-linked. The Y in addition carries a non-homologous portion, which bears the Y chromosome factors passed from a father to all his sons.

With this histological observation and the knowledge of the three kinds of sex linkage in fishes, it was but a step to the conscious search for incompletely sex-linked genes in man. Haldane (1936) made such a search, using recorded pedigrees, and found evidence for the partial sex-linked nature of six genes: total colorblindness, xeradoma pigmentosum, Oguchi's disease, recessive epidermolysis bullosa, and two kinds of retinitis pigmentosa (one recessive unassociated with deafness, the other dominant).

Incompletely sex-linked genes will behave as ordinary autosomal factors in pedigrees except for one thing: some sibships tend to yield too many affected males and normal females, while other sibships yield too many normal males and affected females. In the case of a dominant gene, the affected offspring of affected fathers will tend to be of the same sex as the paternal parent from whom the father received the gene. In the case of a recessive gene the situation is not so obvious, and the requisite statistical analysis is rather intricate.

Thus the partial sex-linked nature of a gene may easily be overlooked in the ordinary analysis of pedigrees. Older known genes must be reanalysed for the possibility of incomplete sex linkage, and all new genes as they are discovered must be subjected to such analysis. Since the gene frequency is usually low for mutant factors in man, crossing over can not be studied between any two genes, and the investigation must concern itself with crossing over between the gene and sex, or, more exactly, between the gene and the unpaired non-homologous portion of the X and Y chromosomes.

In the absence of three-generation pedigrees, incomplete sex linkage may be investigated in paired sib material, using 2×2 tables such as were suggested by Penrose (1935) for autosomal linkage. Having on hand in our laboratory the records of a number of paired sibs tested for blood group, blood type, taste deficiency to phenyl-thio-carbamide and taste deficiency to mercapto-benzo-selenazol, we have set up these data in contingency tables, using the character as one variable and sex as the other. (A paper on the autosomal recessive nature of the taste deficiency to mercapto-benzo-selenazol is now being prepared for publication.)

Chi square was determined by the formula

$$\chi^2 = \frac{n [(ad) - (bc)]^2}{(a + b)(c + d)(a + c)(b + d)}$$

where a = number of pairs alike in both characters,
 b = number of pairs alike in one, unlike in the other,
 c = number of pairs unlike in the one, alike in the other,
 d = number of pairs unlike in both characters,
 n = total number of pairs of sibs.

Tables I to VI, inclusive, present the data in the form of 2 by 2 contingency tests, with the chi square determinations, and the appropriate probabilities with one degree of freedom. It will be seen that in no case is there a significant deviation from proportionality. It can therefore be stated that the genes for the blood groups, the blood types, the taste deficiency to phenyl-thio-carbamide and the taste deficiency to mercapto-benzo-selenazol do not appear to be located on the homologous portions of the sex chromosomes. We are testing this possibility for other factors in man as rapidly as possible.

TABLE I

Agglutininogen A.....	SEX		
		Like	Unlike
	Like	84	52
	Unlike	37	17
		121	69

$$\chi^2 = .076$$

$$P = .95 - .70$$

TABLE II

Agglutininogen B.....	SEX		
		Like	Unlike
	Like	104	62
	Unlike	17	7
		121	69

$$\chi^2 = .061$$

$$P = .95 - .70$$

TABLE III

Agglutininogen M.....	SEX		
		Like	Unlike
	Like	94	55
	Unlike	22	9
		116	64

$$\chi^2 = .070$$

$$P = .95 - .70$$

TABLE IV

Agglutininogen N.....	SEX			
		Like	Unlike	
	Like	83	38	121
	Unlike	33	26	59
		116	64	180

$$\chi^2 = 2.78$$

$$P = .30 - .05$$

TABLE V

Taste P. T. C.....	SEX			
		Like	Unlike	
	Like	93	63	156
	Unlike	42	29	71
		135	92	227

$$\chi^2 = .004$$

$$P = .99$$

TABLE VI

Taste M. B. S.....	SEX			
		Like	Unlike	
	Like	49	44	93
	Unlike	10	15	25
		59	59	118

$$\chi^2 = 1.269$$

$$P = .30 - .05$$

REFERENCES

- Haldane, J. B. S. 1936. *Annals of Eugenics*, 7: 28-57.
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 Penrose, L. S. 1935. *Annals of Eugenics*, 6: 133-138.